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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,298	12/18/2006	M. Ian Phillips	USF-200TCXZ1	6761

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EXAMINER	
SHEN, WU CHENG WINSTON	
ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/567,298	PHILLIPS ET AL.	
	Examiner	Art Unit	
	WU-CHENG Winston SHEN	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-27* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The claim amendments filed on 02/06/2006 have been entered. Claims 3, 6, 8, 11-21, 23, 24, 26, and 27 are amended. Claims 1-27 are pending in the instant application.

It is noted that amended claims 23 and 24 recite "The method of claim 1". However, claim 1 is directed to a product, not a method. Amended claims 23 and 24 are interpreted as "The method of claim 21". Amendments of claims 23 and 24 different from this interpretation will render the claims to be subject to further restriction.

Election/Restrictions

2. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

I. Claims 1-20, drawn to a genetically modified cell comprising: (a) a first exogenous polynucleotide comprising a gene switch/biosensor, wherein said gene switch/biosensor encodes a physiological stimulus-sensitive chimeric transactivator and an operatively linked promoter; and (b) a second exogenous polynucleotide comprising a gene amplification system, wherein said gene

amplification system comprises a nucleic acid sequence encoding a therapeutic product.

II. Claims 21-23, drawn a method for modifying a tissue *in vitro*, the method comprising delivering to the tissue a genetically modified cell of any claim 1.

III. Claims 21, 22, 24 and 25, drawn a method for modifying a tissue *in vivo*, the method comprising delivering to the tissue a genetically modified cell of any claim 1.

IV. Claim 26, drawn to a genetically modified stem cell comprising: (a) a first exogenous polynucleotide comprising: (1) a nucleic acid sequence encoding a GAL4 DNA-binding domain, (2) a nucleic acid sequence encoding an oxygen-dependent degradation (ODD) domain polypeptide, (3) a nucleic acid sequence encoding a p65 activation domain, (4) two AAV ITRs, and (5) an operatively linked promoter; and (b) a second exogenous polynucleotide comprising six copies of a GAL4 UAS, an E1b TATA element, a therapeutic gene, and two AAV ITRs.

V. Claim 27, drawn to a method for modifying a tissue *in vitro*, comprising delivering to the tissue a genetically modified stem cell of claim 26.

VI. Claim 27, drawn to a method for modifying a tissue *in vivo*, comprising delivering to the tissue a genetically modified stem cell of claim 26.

3. The inventions listed as Groups I-XVI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Applicant's claims encompass multiple inventions, multiple products (Groups I and IV) and multiple methods (Groups II-III and V-VI), and do not have a special technical feature which link the inventions one to the other, and lack unity of invention. The common technical feature in all groups is a genetically modified cell comprising two exogenous polynucleotides. However, this common technical feature of a genetically modified cell comprising two exogenous polynucleotides cannot be a special technical feature under PCT Rule 13.2 because the feature is shown in the prior art. For instance, **Fields et al.** (1989) generated a system of two hybrid proteins in yeast containing parts of GAL4: the GAL4 DNA-binding domain fused to a protein 'X' and a GAL4 activating region fused to a protein 'Y' (See abstract and Figure, Fields et al., A novel genetic system to detect protein-protein interactions, *Nature*, 340(6230):245-6, 1989).

4. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

(i) HO-1, superoxide dismutase, phospholanban (PLN) pre-pro-insulin, an anti-cell growth polypeptide, an anti-angiogenesis polypeptide, tPA, erythropoietin, a polypeptide with hypolipidemic activity, a polypeptide that acts on the cholesteryl ester transfer protein and lipase

systems, a polypeptide that provides low density lipoprotein receptor replacement, a polypeptide that induces vascular protection and disobliteration of occlusions, and an interfering RNA molecule (claim 7). The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: They are distinct therapeutic products for different therapies.

(ii) a hematopoeitic stem cell, a mesenchymal stem cell (MSC), a muscle derived stem cell, and a bone marrow mesenchymal progenitor cell (MPC) (claim 13). The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: They are distinct stem cells originated from different tissues with distinct differentiation potentials.

(iii) a muscle cell, a tubular cell of kidney, a type I pneumocyte of lung, a type II pneumocyte of lung, a ependymal cell, a cell from the subventricular zone of the central nervous system, a blood cell, a duct cell of the pancreas, an epidermal cell of the skin, an endothelial cell, a fat cell, an epithelial cell, a neurocell, and a Schwann cell (claim 14). The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: They are different types of differentiated cells performing distinct cellular functions.

(iv) a cytokine, MCP-1, c-reactive protein, elevated triglyceride level, elevated oxidized LDL cholesterol level, elevated Lp(a) level, elevated homocysteine level, decreased HDL level, and decreased nitric oxide production (claim 19). The species listed above do not relate to a

single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: They are different physiological stimuli that lead to distinct physiological responses.

(v) diabetes, cancer, stroke, pulmonary fibrosis, arthritis, atherosclerosis, and inflammation (claim 25). The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: They are different diseased conditions with different pathological conditions caused by different underlying reasons and can be treated by different approaches of therapies.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election. The election of species of **(i)** to **(v)** must be consistent with the election of invention.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

MPEP 1893.03(d) Unity of Invention Rejoinder

5. MPEP 1893.03(d) states: If an examiner (1) determines that the claims lack unity of invention and (2) requires election of a single invention, when all of the claims drawn to the elected invention are allowable (i.e., meet the requirements of 35 U.S.C. 101, 102, 103 and 112), the nonelected invention(s) should be considered for rejoinder. Any nonelected product claim that requires all the limitations of an allowable product claim, and any nonelected process claim that requires all the limitations of an allowable process claim, should be rejoined. See MPEP § 821.04 and § 821.04(a). Any nonelected processes of making and/or using an allowable product should be considered for rejoinder following the practice set forth in MPEP § 821.04(b).

6. Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction were not required because the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the

inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103 (a) of the other invention.

7. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent examiner, Peter Paras, can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you

would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Wu-Cheng Winston Shen/, Ph. D.
Patent Examiner
Art Unit 1632